

GAO

United States General Accounting Office

Report to the Chairmen and Ranking
Minority Members, Committee on Labor
and Human Resources, U.S. Senate, and
Committee on Commerce, House of
Representatives

March 1997

NIH-FUNDED RESEARCH

Therapeutic Human Fetal Tissue Transplantation Projects Meet Federal Requirements



DISSEMINATION STATEMENT A

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Document Unclassified

19970402 066

United States
General Accounting Office
Washington, D.C. 20548

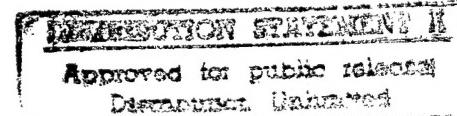
Health, Education, and
Human Services Division

B-276018

March 10, 1997

The Honorable James M. Jeffords
Chairman
The Honorable Edward M. Kennedy
Ranking Minority Member
Committee on Labor and Human Resources
United States Senate

The Honorable Thomas J. Bliley, Jr.
Chairman
The Honorable John D. Dingell
Ranking Minority Member
Committee on Commerce
House of Representatives



Therapeutic human fetal tissue transplantation is a promising area of research that may have application for a broad range of diseases, such as juvenile diabetes and leukemia. Current federally funded research projects use fetal tissue—cells from electively aborted fetuses—to treat patients with Parkinson's disease. Although this research holds promise for treating diseases, concerns have been raised about the acceptance of fetal tissue transplantation; that is, some women might choose to conceive for the sole purpose of aborting their fetuses, so that tissue could be provided to treat family members or to supply fetal material for financial gain.

In March 1988, the Department of Health and Human Services (HHS) imposed a moratorium on the use of federal funds for research projects on therapeutic human fetal tissue transplantation until a panel, appointed by HHS, could study the ethical issues involved.¹ In the fall of 1988, the panel concluded that the use of human fetal tissue in research is acceptable public policy, but the moratorium remained until the President ordered it lifted in January 1993. At the same time, the Secretary, HHS, directed the National Institutes of Health (NIH) to develop interim guidelines for the support and conduct of such research projects "to ensure that federal funding of human fetal tissue transplantation research does not encourage the choice of abortion." In June 1993, the NIH Revitalization Act of 1993 (P.L. 103-43) was enacted, a part of which establishes the conditions under which federally funded therapeutic human fetal tissue transplantation research can take place.²

¹During the moratorium, private funding was used for therapeutic transplantation studies.

²The NIH interim guidelines were withdrawn when P.L. 103-43 was enacted.

The NIH Revitalization Act of 1993 requires us to carry out a compliance review of research on fetal tissue transplantation conducted or supported by HHS. Specifically, the act requires that we (1) determine compliance with informed consent and other documentation and (2) report on any violations occurring in the acquisition of human fetal tissue for use in transplantation.

To determine compliance with the requirements of the act, we met with federal officials and with project personnel at two institutions awarded grants for federally funded research on therapeutic human fetal tissue transplantation. The federal officials gave us information from NIH's Office for Protection from Research Risks (OPRR),³ Office of Science Policy, and the National Institute of Neurological Disorders and Stroke (NINDS). This information included project funding and status, as well as institutional procedures for ensuring protection for human subjects.

We visited the project personnel at the University of Colorado Health Sciences Center in Denver, Colorado, and the Mount Sinai Medical Center in New York City, as well as its affiliated site at the University of South Florida in Tampa, Florida.⁴ We spoke with the principal investigators and the chairs of the institutional review boards.⁵ In addition, we examined documents used for the research projects, including consent forms and statements of the attending physicians. In reviewing such documents, we were mindful of the confidentiality granted to the project participants and of the integrity of the double-blind research methodology. These double-blind research projects were designed so that neither the recipients nor the researchers who evaluate the outcome of the transplant surgery knew which patients were in the experimental group and which in the control group. In our workpapers, we did not record the names of the donors or recipients, nor any of the dates on which the transplants took place. We reviewed the relevant documents to ensure that the proper number of forms were present and that consent had been obtained on or before the dates that transplants were performed.

³OPRR has the responsibility for ensuring that institutions awarded grants for research on fetal tissue transplantation comply with the act's requirements for informed consent and other human subject protection.

⁴The University of South Florida is "affiliated" because it receives funding from Mount Sinai's NIH award. We needed to visit South Florida because it had relevant documents.

⁵Institutional review boards are responsible for examining research proposals and ongoing studies in order to ensure protection of human subjects from risks. These boards, composed mainly of scientists at institutions doing the research, are required to report to the NIH any violations or unanticipated problems involving risks to subjects.

We conducted our review from October 1996 to December 1996 in accordance with generally accepted government auditing standards.

Results in Brief

In general, the requirements of the act are being complied with. The act's documentation requirements—pertaining to informed consent of donors and "donees" (recipients) and compliance statements made by institutions, researchers, and attending physicians—were met. HHS did not submit annual reports on the program's activities, however, as required by the act. But the agency did submit a combined report on January 29, 1997, describing the activities from fiscal years 1993 through 1995.

There have been no reported violations in the acquisition of human fetal tissue for use in transplantation, according to NIH and our verification efforts.

Background

Between fiscal years 1993 and 1996, NIH awarded over \$6 million for five extramural projects involving therapeutic human fetal tissue research. Two projects—at the University of Colorado Health Sciences Center and the Mount Sinai Medical Center—involved actual transplantation of fetal tissue. These projects accounted for about \$5.9 million of the funds. Both were funded by NINDS, which expects to continue funding these projects in fiscal year 1997. The remaining three projects—at Yale University School of Medicine, University of Colorado Health Sciences Center, and Columbia University College of Physicians and Surgeons—totaling about \$280,000, were funded through NIH's National Center for Research Resources (NCRR) grants at General Clinical Research Center (GCRC) sites. For these three projects, funds were not spent to transplant fetal tissue, but to clinically observe Parkinson's patients before and after transplant surgery. (For more detailed funding information, see app. I).

No intramural projects involving therapeutic human fetal tissue transplantation have been funded. At the time of our review, no new projects on therapeutic human fetal tissue transplantation were being proposed for funding by January 1997.

Ongoing Projects Have Complied With the Requirements of the Act

The act contains the following eight requirements for research on human fetal tissue transplantation:

(1) Informed consent of the donor: The woman providing the tissue must make a signed written statement, declaring that she is donating fetal tissue for research, without any restrictions on, or awareness of, who the tissue recipient will be.

(2) Attending physician statement: The physician responsible for obtaining the tissue from the woman involved must make a signed written statement declaring that

- in the case of tissue obtained through an induced abortion, consent for the abortion preceded consent for the tissue donation, the timing of the abortion was not solely for purposes of obtaining the tissue, and the abortion was performed in accordance with state law;
- the woman gave informed consent, as described in (1) above; and
- the donor was given full disclosure of any interest the physician has in the research use of the tissue and any known medical risks and privacy risks associated with the tissue donation.

(3) Principal researcher statement: The individual with the principal responsibility for conducting the research must make a signed written statement indicating awareness that the tissue obtained is human tissue, that it may have been obtained through a spontaneous or induced abortion or a stillbirth,⁶ and that it was donated for research purposes. The statement also must indicate that the researcher

- has provided such information to others with responsibilities for the research,
- will obtain written acknowledgment from the tissue recipient of the receipt of such information, and
- has not been involved in the timing of, or method used, in the abortion.

(4) Informed consent of the recipient: The individual to be a recipient of a transplantation of tissue must provide written acknowledgment, as described in (3) above.

⁶Due to concerns about the quality of the tissue, only tissue obtained from induced abortions is used in research on therapeutic human fetal tissue transplantation.

(5) Availability of statements for audit: The head of each agency or entity conducting the research must certify to the Secretary of HHS that the required statements (1 to 4) will be available for audit by the Secretary.

(6) Compliance with state law: The recipients of funding for research on fetal tissue transplantation must agree to conduct research in accordance with applicable state law.

(7) HHS annual report: HHS is required to submit annual reports to the House Committee on Commerce and the Senate Committee on Labor and Human Resources, describing the fetal tissue transplantation activities carried out during the preceding fiscal year and discussing whether those activities were carried out in accordance with the law.

(8) Tissue purchase and donation restrictions: The purchase of human fetal tissue is prohibited. In addition, donated tissue can not be transplanted into a recipient specified by the donor, such as a relative of the donor, nor can a person acquiring tissue pay costs associated with the abortion. Violators are subject to fines or imprisonment or both.

In general, the research projects we reviewed were in compliance with the requirements of the act. See table 1 for a summary of our methodology and findings, which verify compliance.

Table 1: GAO Verification of Compliance With Requirements of the Act

| Requirement of the act | Methodology and findings |
|---|--|
| (1) Informed consent of donor (2) Attending physician statement (3) Principal researcher statement (4) Informed consent of recipient | We checked for the inclusion of the required statements on the forms used by the projects, ^a and verified that the required forms were in the project files and were properly executed. Documentation for both projects met the requirements of the law. |
| (5) Availability of statements for audit | We checked whether the institutions involved in this research had submitted institutional assurances to NIH that covered the audit requirements. Each institution involved had submitted such an assurance. |
| (6) Compliance with state law | We checked whether the institutions involved in this research had submitted institutional assurances to NIH that covered the state law requirements. Each institution involved had submitted such an assurance. |
| (7) HHS annual report | We checked on HHS submission of reports to the Congress. HHS was not in compliance with the annual requirement. The agency submitted a combined report covering fiscal years 1993-95 in January 1997. |
| (8) Tissue purchase and donation restrictions | We checked with NIH's OPRR and the funded institutions' institutional review boards. No violations had been reported or detected. |

^aEach project had several participating institutions, but only one institution for each project was listed as the funded institution.

We found that the two research projects on fetal tissue transplantation adhered to the documentation requirements for the protection of human subjects. Our examination of the four forms used by each of the two projects conducting fetal tissue transplantation research indicated that the requirements of the law were met. During our visits to the project sites, we also verified that the forms had been appropriately executed for each project. All of the forms that were required were present, signed, dated, and witnessed.

To date, NIH's OPRR has not performed audits on the two projects conducting fetal tissue transplantation research because there have been no complaints reported. According to OPRR, NIH funds approximately 15,000 studies involving human subjects and OPRR can only carry out about five compliance site visits each year. Therefore, site visits tend to be made to institutions with some indication of problems.

We also found that the Secretary, HHS, had not submitted annual reports to your Committees as required. NIH prepared draft annual reports for fiscal

years 1993, 1994, and 1995 and forwarded them to the Secretary in May 1994, June 1995, and August 1996, respectively. HHS submitted a combined report, covering fiscal years 1993 through 1995, on January 29, 1997.

Agency Comments

A draft of this report was reviewed by NIH officials. They agreed with our findings related to therapeutic human fetal tissue transplantation research. Based on these officials' technical comments, we changed the report where appropriate.

We are sending copies of this report to other interested Members of Congress, and will make copies available to others on request. Please call me on (202) 512-7119 if you or your staff have any questions about the issues discussed above. Other major contributors include Rosamond Katz, Erwin Bedarf, Ann White, and Robert Crystal.



Bernice Steinhardt
Director, Health Services Quality
and Public Health Issues

NIH Funding of Award Institutions for Research on Fetal Tissue Transplantation, FYs 1993-96

| Award institution | NIH sponsor | FY 1993 | FY 1994 | FY 1995 | FY 1996 ^a | Total NCRR FYs 1993-96 | Total NINDS FYs 1993-96 | Total FYs 1993-96 |
|--|-------------|-----------------|--------------------|--------------------|----------------------|------------------------|-------------------------|--------------------|
| Yale University School of Medicine | | | | | | | | \$213,357 |
| | NCRR (GCRC) | \$97,325 | \$76,693 | \$36,007 | \$3,332 | \$213,357 | | b |
| University of Colorado Health Sciences Center^c | | | | | | | | 3,855,445 |
| | NINDS | d | 1,019,956 | 1,326,627 | 1,507,573 | | b | 3,854,156 |
| | NCRR (GCRC) | d | d | 1,289 | d | 1,289 | | b |
| Columbia University College of Physicians and Surgeons | | | | | | | | 66,890 |
| | NCRR (GCRC) | d | d | 26,424 | 40,466 | 66,890 | | b |
| Mount Sinai Medical Center^{c,e} | | | | | | | | 2,028,049 |
| | NINDS | d | d | 952,070 | 1,075,979 | | b | 2,028,049 |
| Total | | \$97,325 | \$1,096,649 | \$2,342,417 | \$2,627,350 | \$281,536 | \$5,882,205 | \$6,163,741 |

^aOnly preliminary information was available for FY 1996.

^bTotal not applicable here.

^cThese funds were used for a research project involving transplant surgery.

^dNo funding.

^eThe University of South Florida was funded through this award.

Source: Office of Science Policy, NIH.